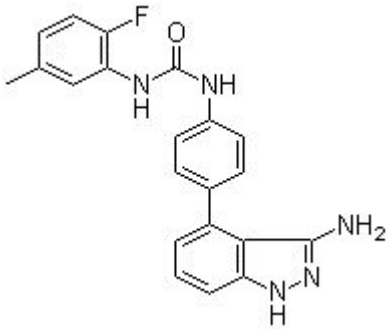
Product Introduction

Linifanib (ABT-869)

Linifanib (ABT-869) is a novel, potent ATP-competitive **VEGFR/PDGFR** inhibitor for **KDR**, **CSF-1R**, **Flt-1/3** and PDGFRβ with **IC50** of 4 nM, 3 nM, 3 nM/4 nM and 66 nM respectively, mostly effective in mutant kinase-dependent cancer cells (i.e. FLT3). Phase 3.

Technical Data:

Molecular Weight (MW):	375.41	
Formula:	$C_{21}H_{18}FN_5O$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 75 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	796967-16-3	

Biological Activity

Linifanib shows inhibitory to Kit, PDGFRβ and Flt4 with IC50 of 14 nM, 66 nM and 190 nM in kinases assay. Linifanib also inhibits ligand-induced KDR, PDGFRβ, Kit, and CSF-1R phosphorylation with IC50 of 2 nM, 2 nM, 31 nM and 10 nM at cellular level and this cellular potency could be affected by serum protein. Linifanib suppresses VEGF-stimulated HUAEC proliferation with IC50 of 0.2 nM. While Linifanib has weak activity against tumor cells which are not induced by VEGF or PDGF, except for MV4-11 leukemia cells

(with constitutively active form of Flt3) with IC50 of 4 nM. Linifanib could cause a decrease in S and G2-M phases with a corresponding increase in the sub-G0-G1 apoptotic population in MV4-11 cells. [1] Linifanib binds to the ATP-binding site of CSF-1R with K_i of 3 nM. [2] Linifanib (10 nM) exhibits a reduced phosphorylation of Akt at Ser473 and decreased phosphorylation of GSK3βat Ser9 in Ba/F3 FLT3 ITD cell lines. [3]

Linifanib (0.3 mg/kg) results in complete inhibition of KDR phosphorylation in lung tissue. Linifanib also inhibits the edema response with ED50 of 0.5 mg/kg. Linifanib (7.5 and 15 mg/kg, bid) significantly inhibits both bFGF- and VEGF-induced angiogenesis in the cornea. Linifanib inhibits tumor growth in flank xenograft models including HT1080, H526, MX-1 and DLD-1 with ED75 from 4.5-12 mg/kg. Linifanib also shows efficacy in A431 and MV4-11 xenografts at low dose levels. Linifanib (12.5 mg/kg bid) reveals a decrease of microvasculure density in MDA-231 xenograft. Linifanib shows a C_{max} and $AUC_{24\ hours}$ with 0.4 μg/mL and 2.7 μg•hour/mL in HT1080 fibrosarcoma model. [1]

References

[1] Albert DH, et al. Mol Cancer Ther, 2006, 5(4), 995-1006.

[2] Guo J, et al. Mol Cancer Ther, 2006, 5(4), 1007-1013.

[3] Hernandez-Davies JE, et al. Mol Cancer Ther, 2011, 10(6), 949-959.

[4] Jasinghe VJ, et al. J Hepatol. 2008, 49(6), 985-997.

[5] Albert DH, et al. Mol Cancer Ther. 2006, 5(4), 995-1006.

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